# 10/540546

09598

JC17 Rec'd PCT/PTO 24 JUN 2005

<110> Fujisawa Pharmaceutical Co., Ltd.	
<120> New methods for selecting an immunosuppressive agent	
<130> 09598	
<150> JP2002-378800 <151> 2002-12-27	
<160> 86	
<170> Patentin version 3.1	
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cca Pro	Asp	gag Glu 1075	gag d Glu l	occ a Pro M	etg (	Glu (	gag ( Glu (	gag ( Glu l	ccg ( Pro l	occ o Pro l	etg Leu	tag				3255

- (211) 1084
- ₹212> PRT
- <213> Homo sapiens

**<400> 2** 

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Val Glu Leu Leu Asn Pro Ala Arg Val Asn His Met Pro Ser Thr Val 20 25 30

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Met Asp Leu Arg Leu Asp His Gin Phe Ser Leu Pro Val Ala Giu Pro 50 60

Ala Leu Arg Glu Gln Gln Leu Gln Gln Glu Leu Leu Ala Leu Lys Gln 65 70 75 80

Lys Gin Gin lie Gin Arg Gin lie Leu lie Ala Giu Phe Gin Arg Gin 85 90 95

His Glu Gln Leu Ser Arg Gln His Glu Ala Gln Leu His Glu His Ile 100 105 110

Lys Gin Gin Giu Met Leu Ala Met Lys His Gin Gin Giu Leu Leu 115 120 125

Glu His Gln Arg Lys Leu Glu Arg His Arg Gln Glu Gln Glu Leu Glu 130 135 140

Lys Gln His Arg Glu Gln Lys Leu Gln Gln Leu Lys Asn Lys Glu Lys 145 155 160

Gly Lys Glu Ser Ala Val Ala Ser Thr Glu Val Lys Met Lys Leu Gin 165 170 175

Glu Phe Val Leu Asn Lys Lys Lys Ala Leu Ala His Arg Asn Leu Asn 180 185 190

His Cys IIe Ser Ser Asp Pro Arg Tyr Trp Tyr Gly Lys Thr Gln His 195 200 205

Ser Ser Leu Asp Gin Ser Ser Pro Pro Gin Ser Giy Vai Ser Thr Ser 210 215 220

Tyr Asn His Pro Val Leu Gly Met Tyr Asp Ala Lys Asp Asp Phe Pro 225 230 240

Leu Arg Lys Thr Ala Ser Glu Pro Asn Leu Lys Leu Arg Ser Arg Leu 245 250 255

Lys Gin Lys Val Ala Giu Arg Arg Ser Ser Pro Leu Leu Arg Arg Lys 260 265 270

Asp Gly Pro Val Val Thr Ala Leu Lys Lys Arg Pro Leu Asp Val Thr 275 280 285

Asp Ser Ala Cys Ser Ser Ala Pro Gly Ser Gly Pro Ser Ser Pro Asn 290 295 300

Asn Ser Ser Gly Ser Val Ser Ala Glu Asn Gly IIe Ala Pro Ala Val 305 310 315 320

Pro Ser IIe Pro Ala Giu Thr Ser Leu Ala His Arg Leu Val Ala Arg 325 330 335

Glu Gly Ser Ala Ala Pro Leu Pro Leu Tyr Thr Ser Pro Ser Leu Pro 340 345 350

Asn IIe Thr Leu Gly Leu Pro Ala Thr Gly Pro Ser Ala Gly Thr Ala 355 360 365

Gly Gin Gin Asp Thr Glu Arg Leu Thr Leu Pro Ala Leu Gin Gin Arg

Leu Ser Leu Phe Pro Gly Thr His Leu Thr Pro Tyr Leu Ser Thr Ser 385 395 400

Pro Leu Glu Arg Asp Gly Gly Ala Ala His Ser Pro Leu Leu Gln His 405 410 415

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420 425 430

Leu Gly Ala Leu Pro Leu His Ala Gln Ser Leu Val Gly Ala Asp Arg 435 440 445

Val Ser Pro Ser Ile His Lys Leu Arg Gln His Arg Pro Leu Gly Arg 450 455 460

Thr Gin Ser Ala Pro Leu Pro Gin Asn Ala Gin Ala Leu Gin His Leu 465 470 475 480

Val lle Gin Gin His Gin Gin Phe Leu Giu Lys His Lys Gin Gin 485 490 495

Phe Gin Gin Gin Leu Gin Met Asn Lys IIe IIe Pro Lys Pro Ser 500 505 510

Glu Pro Ala Arg Gln Pro Glu Ser His Pro Glu Glu Thr Glu Glu Glu 515 520 525

Leu Arg Glu His Gln Ala Leu Leu Asp Glu Pro Tyr Leu Asp Arg Leu 530 540

Pro Gly Gln Lys Glu Ala His Ala Gln Ala Gly Val Gln Val Lys Gln 545 550 555 560

Glu Pro Ile Glu Ser Asp Glu Glu Glu Ala Glu Pro Pro Arg Glu Val 565 570 575

Glu Pro Gly Gln Arg Gln Pro Ser Glu Glu Leu Leu Phe Arg Gln 580 585 590

Gin Ala Leu Leu Giu Gin Gin Arg IIe His Gin Leu Arg Asn Tyr 595 600 605

Gin Ala Ser Met Giu Ala Ala Giy Ile Pro Val Ser Phe Giy Giy His 610 615 620

Arg Pro Leu Ser Arg Ala Gin Ser Ser Pro Ala Ser Ala Thr Phe Pro 625 630 635 640

Val Ser Val Gin Giu Pro Pro Thr Lys Pro Arg Phe Thr Thr Giy Leu 645 650 655

Val Tyr Asp Thr Leu Met Leu Lys His Gln Cys Thr Cys Gly Ser Ser 660 665 670

Ser Ser His Pro Glu His Ala Gly Arg IIe Gln Ser IIe Trp Ser Arg 675 680 685

Leu Gin Giu Thr Giy Leu Arg Giy Lys Cys Giu Cys Iie Arg Giy Arg 690 695 700

Lys Ala Thr Leu Glu Glu Leu Gln Thr Val His Ser Glu Ala His Thr 705 710 715 720

Leu Leu Tyr Gly Thr Asn Pro Leu Asn Arg Gln Lys Leu Asp Ser Lys 725 730 735

Lys Leu Leu Giy Ser Leu Ala Ser Val Phe Val Arg Leu Pro Cys Gly 740 745 750

Gly Val Gly Val Asp Ser Asp Thr IIe Trp Asn Glu Val His Ser Ala 755 760 765

Gly Ala Ala Arg Leu Ala Val Gly Cys Val Val Glu Leu Val Phe Lys

775

Val Ala Thr Gly Glu Leu Lys Asn Gly Phe Ala Val Val Arg Pro Pro

Gly His His Ala Glu Glu Ser Thr Pro Met Gly Phe Cys Tyr Phe Asn 805 810 815

Ser Val Ala Val Ala Ala Lys Leu Leu Gin Gin Arg Leu Ser Val Ser

Lys lie Leu lie Val Asp Trp Asp Val His His Gly Asn Gly Thr Gin 835 840 845

Gin Ala Phe Tyr Ser Asp Pro Ser Val Leu Tyr Met Ser Leu His Arg 850 855 860

Tyr Asp Asp Gly Asn Phe Phe Pro Gly Ser Gly Ala Pro Asp Glu Val 865 870 875 880

Gly Thr Gly Pro Gly Val Gly Phe Asn Val Asn Met Ala Phe Thr Gly 885 890 895

Gly Leu Asp Pro Pro Met Gly Asp Ala Glu Tyr Leu Ala Ala Phe Arg 900 905 910

Thr Val Val Met Pro ile Ala Ser Giu Phe Ala Pro Asp Val Val Leu 915 920 925

Val Ser Ser Gly Phe Asp Ala Val Glu Gly His Pro Thr Pro Leu Gly 930 935 940

Gly Tyr Asn Leu Ser Ala Arg Cys Phe Gly Tyr Leu Thr Lys Gln Leu 945 950 955 960

Met Gly Leu Ala Gly Gly Arg Ile Val Leu Ala Leu Glu Gly Gly His 965 970 975

Asp Leu Thr Ala lie Cys Asp Ala Ser Giu Ala Cys Val Ser Ala Leu 980 985 990

Leu Gly Asn Glu Leu Asp Pro Leu Pro Glu Lys Val Leu Gln Gln Arg

Pro Asn Ala Asn Ala Val Arg Ser Met Glu Lys Val Met Glu lle His 1015

Ser Lys Tyr Trp Arg Cys Leu Gin Arg Thr Thr Ser Thr Ala Gly Arg 1025 1030 1035 1046

Ser Leu lle Glu Ala Gln Thr Cys Glu Asn Glu Glu Ala Glu Thr Val

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Pro Asp Glu Glu Pro Met Glu Glu Glu Pro Pro Leu

<210>

〈211〉 〈212〉 3255

DNA <213> Artificial

**<220>** 

**〈221〉** CDS

**〈222〉** (1).. (3255)

Dominant negative mutant (H802K, H803L) of human histone deacetylase-4 (HDAC4) gene

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															g ccc I Pro	144
															g ccg u Pro	192
															cag Gin 80	240
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				Ser					Ala					His	atc	336
			GIn					Met							ctg Leu	384
		Gin													gag Glu	432
	Gln		cgg Arg												aag Lys 160	480
			agt Ser													528
			ctc Leu 180													576
			tcc Ser													624
agt Ser	tcc Ser 210	ctt Leu	gac Asp	cag Gin	agt Ser	tct Ser 215	cca Pro	ccc Pro	cag Gin	agc Ser	gga Gly 220	gtg Val	tcg Ser	acc Thr	tcc Ser	672
tat Tyr 225	aac Asn	cac His	ccg Pro	gtc Val	ctg Leu 230	gga Gly	atg Met	tac Tyr	gac Asp	gcc Ala 235	aaa Lys	gat Asp	gac Asp	ttc Phe	cct Pro 240	720
			aca Thr													768
			gtg Val 260				Arg					Leu				816
			gtg Val			Ala					Pro					864
Asp			tgc Cys		Ser					Gly						912
aac Asn	agc Ser	tcc Ser	ggg Gly	agc Ser	gtc : Val :	agc ( Ser /	gcg . Ala	gag Glu	aac Asn	ggt a Gly	atc lle	gcg Ala	ccc Pro	gcc Ala	gtc Val	960

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305					31	0				31	5				320	)
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aaa Lys	ctt Leu	cta Lei	a gg u Gi: 74	y Sei	cto Leu	gcc Ala	Ser	gtg Val 745	Phe	gtc Val	ogg Arg	Leu	750	Cys	ggt	2256
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09598	
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gac ctg acc gcc att tgc gac gcc tcg gaa gca tgt gtt tct gcc ttg Asp Leu Thr Ala lie Cys Asp Ala Ser Giu Ala Cys Val Ser Ala Leu 980 985 990	2976
ctg gga aac gag ctt gat cct ctc cca gaa aag gtt tta cag caa aga Leu Gly Asn Glu Leu Asp Pro Leu Pro Glu Lys Val Leu Gln Gln Arg 995 1000 1005	3024
ccc aat gca aac gct gtc cgt tcc atg gag aaa gtc atg gag atc cac Pro Asn Ala Asn Ala Val Arg Ser Met Glu Lys Val Met Glu lie His 1010 1015 1020	3072
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tct ctg atc gag gct cag act tgc gag aac gaa gaa gcc gag acg gtc 3 Ser Leu IIe Glu Ala Gin Thr Cys Glu Asn Glu Glu Ala Glu Thr Val 1045 1050 1055	168
acc gcc atg gcc tcg ctg tcc gtg ggc gtg aag ccc gcc gaa aag aga Thr Ala Met Ala Ser Leu Ser Val Gly Val Lys Pro Ala Glu Lys Arg 1060 1065 1070	216
cca gat gag gag ccc atg gaa gag gag ccg ccc ctg tag  Pro Asp Giu Giu Pro Met Giu Giu Giu Pro Pro Leu  1075  1080	255
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Asp Val Ala Thr Ala Leu Pro Leu Gin Val Ala Pro Ser Ala Val Pro 35 40 45	
Met Asp Leu Arg Leu Asp His Gin Phe Ser Leu Pro Val Ala Giu Pro 50 55 60	
Ala Leu Arg Glu Gin Gin Leu Gin Gin Glu Leu Leu Ala Leu Lys Gin 65 70 75 80	
Lys Gin Gin He Gin Arg Gin He Leu He Ala Giu Phe Gin Arg Gin 85 90 95	
His Glu Gln Leu Ser Arg Gln His Glu Ala Gln Leu His Glu His Ile 100 105 110	

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- Glu His Gln Arg Lys Leu Glu Arg His Arg Gln Glu Gln Glu Leu Glu 130 135 140
- Lys Gln His Arg Glu Gln Lys Leu Gln Gln Leu Lys Asn Lys Glu Lys 145 155 160
- Gly Lys Glu Ser Ala Val Ala Ser Thr Glu Val Lys Met Lys Leu Gin 165 170 175
- Glu Phe Val Leu Asn Lys Lys Lys Ala Leu Ala His Arg Asn Leu Asn 180 185 190
- His Cys IIe Ser Ser Asp Pro Arg Tyr Trp Tyr Gly Lys Thr Gln His 195 200 205
- Ser Ser Leu Asp Gin Ser Ser Pro Pro Gin Ser Giy Val Ser Thr Ser 210 215 220
- Tyr Asn His Pro Val Leu Gly Met Tyr Asp Ala Lys Asp Asp Phe Pro 225 230 235 240
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- Lys Gin Lys Vai Ala Giu Arg Arg Ser Ser Pro Leu Leu Arg Arg Lys 260 265 270
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- Asp Ser Ala Cys Ser Ser Ala Pro Gly Ser Gly Pro Ser Ser Pro Asn 290 295 300
- Asn Ser Ser Gly Ser Val Ser Ala Glu Asn Gly IIe Ala Pro Ala Val 305 310 315 320
- Pro Ser Ile Pro Ala Glu Thr Ser Leu Ala His Arg Leu Val Ala Arg 325 330 335
- Glu Gly Ser Ala Ala Pro Leu Pro Leu Tyr Thr Ser Pro Ser Leu Pro 340 345 350
- Asn IIe Thr Leu Gly Leu Pro Ala Thr Gly Pro Ser Ala Gly Thr Ala 355 360 365
- Gly Gln Gln Asp Thr Glu Arg Leu Thr Leu Pro Ala Leu Gln Gln Arg 370 375 380
- Leu Ser Leu Phe Pro Gly Thr His Leu Thr Pro Tyr Leu Ser Thr Ser 385 390 395 400
- Pro Leu Glu Arg Asp Gly Gly Ala Ala His Ser Pro Leu Leu Gln His 405 410 415
- Met Val Leu Leu Glu Gin Pro Pro Ala Gin Ala Pro Leu Val Thr Gly
  420 425 430
- Leu Gly Ala Leu Pro Leu His Ala Gln Ser Leu Val Gly Ala Asp Arg 435 440 445
- Val Ser Pro Ser Ile His Lys Leu Arg Gln His Arg Pro Leu Gly Arg 450 455 460
- Thr Gln Ser Ala Pro Leu Pro Gln Asn Ala Gln Ala Leu Gln His Leu 465 470 475 480
- Val lie Gin Gin His Gin Gin Phe Leu Giu Lys His Lys Gin Gin 485 490 495
- Phe Gin Gin Gin Leu Gin Met Asn Lys lie lie Pro Lys Pro Ser 500 505 510

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- Leu Arg Glu His Gln Ala Leu Leu Asp Glu Pro Tyr Leu Asp Arg Leu 530 535 540
- Pro Gly Gln Lys Glu Ala His Ala Gln Ala Gly Val Gln Val Lys Gln 545 555 560
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- Giu Pro Giy Gin Arg Gin Pro Ser Giu Gin Giu Leu Leu Phe Arg Gin 580 585 590
- Gin Ala Leu Leu Giu Gin Gin Arg He His Gin Leu Arg Asn Tyr 595 600 605
- Gin Ala Ser Met Giu Ala Ala Giy IIe Pro Val Ser Phe Giy Giy His 610 615 620
- Arg Pro Leu Ser Arg Ala Gin Ser Ser Pro Ala Ser Ala Thr Phe Pro 625 630 635 640
- Val Ser Val Gin Giu Pro Pro Thr Lys Pro Arg Phe Thr Thr Gly Leu 645 650 655
- Val Tyr Asp Thr Leu Met Leu Lys His Gln Cys Thr Cys Gly Ser Ser 660 665 670
- Ser Ser His Pro Glu His Ala Gly Arg IIe Gln Ser IIe Trp Ser Arg 675 680 685
- Leu Gin Giu Thr Giy Leu Arg Giy Lys Cys Giu Cys Ile Arg Giy Arg 690 695 700
- Lys Ala Thr Leu Glu Glu Leu Gln Thr Val His Ser Glu Ala His Thr 705 710 715 720
- Leu Leu Tyr Gly Thr Asn Pro Leu Asn Arg Gln Lys Leu Asp Ser Lys 725 730 735
- Lys Leu Leu Gly Ser Leu Ala Ser Val Phe Val Arg Leu Pro Cys Gly 740 745 750
- Gly Val Gly Val Asp Ser Asp Thr lle Trp Asn Glu Val His Ser Ala 755 760 765
- Gly Ala Arg Leu Ala Val Gly Cys Val Val Glu Leu Val Phe Lys 770 775 780
- Val Ala Thr Gly Glu Leu Lys Asn Gly Phe Ala Val Val Arg Pro Pro 785 790 795 800
- Gly Lys Leu Ala Glu Glu Ser Thr Pro Met Gly Phe Cys Tyr Phe Asn 805 810 815
- Ser Val Ala Val Ala Ala Lys Leu Gin Gin Arg Leu Ser Val Ser 820 825 830
- Lys lle Leu lle Val Asp Trp Asp Val His His Gly Asn Gly Thr Gln 835 840 845
- Gln Ala Phe Tyr Ser Asp Pro Ser Val Leu Tyr Met Ser Leu His Arg 850 855 860
- Tyr Asp Asp Gly Asn Phe Phe Pro Gly Ser Gly Ala Pro Asp Glu Val 865 870 875 880
- Gly Thr Gly Pro Gly Val Gly Phe Asn Val Asn Met Ala Phe Thr Gly 885 890 895
- Gly Leu Asp Pro Pro Met Gly Asp Ala Glu Tyr Leu Ala Ala Phe Arg 900 905 910

The	- Va	l Va 91		t Pro	0 110	e Ala	a Sei 920		J Pho	e Al	a Pr	o As 92		l Va	l Leu	ı	
Va	936		r GI	y Pho	a Ası	A   6   93		l Glu	ı Giy	y His	s Pro 94	_	r Pr	o Le	u Gly	,	
G13 945		r As	n Le	u Sei	- Ala 950		g Cys	s Phe	Gly	7 Ty:		u Thi	r Ly	s GI	n Leu 960		
Met	Gly	y Le	u Ala	a Gly 965		/ Ari	g Ile	e Val	Let 970		a Lei	ı Glı	ı Gi	y GI: 97	y His 5	•	
Asp	Lei	J Thi	r Ala 980		e Cys	s Asp	Ala	985	_	ı Ala	а Су:	s Va	99	_	a Leu	ı	
Leu	Gly	/ Ası 99!		ı Let	ı Asp	Pro	Let 100		Glu	ı Lys	s Vai		u Gli 205	n Gli	n Arg		
Pro	Asr 101		a Ası	n Ala	Val	Arg 101		Met	: GIL	ı Lys	Va 102		Gli	ı He	e His		
Ser 102		Туғ	Tr	Arg	Cys 103		Glr	Arg	Thr	Thr 103		Thr	- Ala	a Gly	/ Arg 104		
Ser	Leu	ılle	G I L	104		Thr	Cys	Glu	105		Glu	ıAla	Glu	105	- Val 55		
Thr	Ala	Met	: Ala 106		Leu	Ser	Val	G!y 106		Lys	Pro	Ala	107		Arg		
Pro	Asp	107		ı Pro	Met	Glu	108	Glu O	Pro	Pro	Leu	1					
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gat Asp	gtg Val	gcc Ala 35	acg Thr	gcg Ala	ctg Leu	cct Pro	ctg Leu 40	caa Gin	gtg Val	gcc Ala	ccc Pro	tcg Ser 45	gca Ala	gtg Val	ccc Pro	144	
								ttc Phe								192	
gcc Ala 65	ctg Leu	cgg Arg	gag Glu	cag Gin	cag Gin 70	ctg Leu	cag Gin	cag Gin	gag Glu	ctc Leu 75	ctg Leu	gcg Ala	ctc Leu	aag Lys	cag Gin 80	240	
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ccc ttg gag cgg gac gga ggg gca gcg cac agc cct ctt ctg cag cac Pro Leu Glu Arg Asp Gly Gly Ala Ala His Ser Pro Leu Leu Gln His 405 410 415

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		Pro					Leu					Pro			cgg Arg	1392
	Gln					Pro					Ala				ctg Leu 480	1440
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gag Glu	cca Pro	gcc Ala 515	cgg Arg	cag Gin	ccg Pro	gag Glu	agc Ser 520	cac His	ccg Pro	gag Glu	gag Glu	acg Thr 525	gag Glu	gag Glu	gag Glu	1584
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						cac His										1680
						gag Glu										1728
						ccc Pro										1776
						cag Gin										1824
cag Gin	gcg Ala 610	tcc Ser	atg Met	gag Glu	gcc Ala	gcc Ala 615	ggc Gly	atc Ile	ccc Pro	gtg Val	tcc Ser 620	ttc Phe	ggc Gly	ggc Gly	cac His	1872
						cag Gin										1920
						ccc Pro		Lys								1968
		Asp				ctg Leu	Lys					Cys				2016
agc Ser	Ser										Ser					2064
ctg Leu					Leu					Glu						2112
aag Lys	gcc Ala	acc Thr	ctg Leu	gag Glu	gag Glu	cta ( Leu (	cag Gin	acg Thr	gtg Val	cac His	tcg Ser	Glu	gcc Ala (16)	cac His	acc Thr	2160

705					710					711	-		0959	98	700	
705	•				710	,				71!	•				720	
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				Ser					Phe					Cys	ggt Gly	2256
			Val					· He					His		g gcg Ala	2304
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	Ala					L.ys					Val				Pro 800	2400
					Ğlu					Gly					aac Asn	2448
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ggc Gly 945				Ser								acg Thr				2880
atg Met			Ala													2928
gac Asp		Thr					Āla									2976
ctg Leu	Gly					Pro		Pro					Gin			3024
ccc a	aat	gca	aac	gct	gtc	cgt	tcc	atg	gag	aaa	gtc	atg	gag	atc	cac	3072

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Pro	10		a As	n Al	a Va	1 Ar.		r Me	t GI	u Ly		1 Me 20	t GI	u II	e His	<b>!</b>		
	Ly					s Le					r Se				g cgt y Arg 104	:_	120	
tc1 Ser	t ct	g ato u lie	e Gi	g gc I Ala 104	a_Gi	g ac n Thi	t tge r Cya	s Gli	g aa u Asi 10	n Gi	a ga u Gi	a gc u Ala	c ga a Gl	g ac u Th 10	g gtc r Val 55	3	168	
acc Thr	gce Ala	c atg a Met	g gcd E Ala 106	a Se	g cti Lei	g too J Sei	gtø Val	g gg Gly 100	y Va	g aa I Ly	g cc s Pr	c gco	ga: a Gli 10	u Ly	g aga s Arg	3:	216	
		t gag o Glu 107	ı Gir					Gli					ζ			32	255	
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	0> Ser		Gln	Ser 5	His	Pro	Asp	Gly	Leu 10	ı Ser	- Gly	Arg	( Asp	G r 15	) Pro			
Val	Glu	Leu	Leu 20	Asn	Pro	Ala	Arg	Va I 25	Asn	His	Met	Pro	Ser 30	Thr	Val			
Asp	Val	Ala 35	Thr	Ala	Leu	Pro	Leu 40	Gln	Val	Ala	Pro	Ser 45	Ala	Val	Pro			
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Lys	Gin	Gln	He	GIn 85	Arg	Gin	He	Leu	lle 90	Ala	Glu	Phe	GIn	Arg 95	GIn			
His	Glu	Gin	Leu 100	Ser	Arg	GIn	His	Glu 105	Ala	GIn	Leu	His	Glu 110	His	He			
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Glu	His 130	Gln	Arg	Lys	Leu	Glu 135	Arg	His	Arg	GIn	Glu 140	Gin	Glu	Leu	Glu			
Lys 145	Gin	His	Arg	Glu	GIn 150	Lys	Leu	GIn	Gin	Leu 155	Lys	Asn	Lys	Glu	Lys 160			
Gly	Lys	Glu	Ser	Ala 165	Val	Ala	Ser	Thr	Glu 170	Val	Lys	Met	Lys	Leu 175	Gin			
Glu	Phe		Leu 180	Asn	Lys	Lys	Lys	Ala 185	Leu	Ala	His	Arg	Asn 190	Leu	Asn			
His	Cys	i le 195	Ser	Ser	Asp	Pro	Arg 200	Tyr	Trp	Tyr	Gly	Lys 205	Thr	Gin	His			
Ser	Ser 210	Leu	Asp	Gin	Ser	Ser 215	Pro	Pro	GIn	Ser	Gly 220	Val	Ser	Thr	Ser			

Tyr Asn His Pro Val Leu Gly Met Tyr Asp Ala Lys Asp Asp Phe Pro 225 235 240

Leu Arg Lys Thr Ala Ser Glu Pro Asn Leu Lys Leu Arg Ser Arg Leu 245 250 255

Lys Gln Lys Val Ala Glu Arg Arg Ser Ser Pro Leu Leu Arg Arg Lys 260 265 270

Asp Gly Pro Val Val Thr Ala Leu Lys Lys Arg Pro Leu Asp Val Thr 275 280 285

Asp Ser Ala Cys Ser Ser Ala Pro Gly Ser Gly Pro Ser Ser Pro Asn 290 295 300

Asn Ser Ser Gly Ser Val Ser Ala Glu Asn Gly IIe Ala Pro Ala Val 305 310 315 320

Pro Ser IIe Pro Ala Glu Thr Ser Leu Ala His Arg Leu Val Ala Arg 325 330 335

Glu Gly Ser Ala Ala Pro Leu Pro Leu Tyr Thr Ser Pro Ser Leu Pro 340 345 350

Asn IIe Thr Leu Giy Leu Pro Ala Thr Giy Pro Ser Ala Giy Thr Ala 355 360 365

Gly Gln Gln Asp Thr Glu Arg Leu Thr Leu Pro Ala Leu Gln Gln Arg 370 375 380

Leu Ser Leu Phe Pro Gly Thr His Leu Thr Pro Tyr Leu Ser Thr Ser 385 390 395 400

Pro Leu Glu Arg Asp Gly Gly Ala Ala His Ser Pro Leu Leu Gln His 405 410 415

Met Vai Leu Leu Giu Gin Pro Pro Ala Gin Ala Pro Leu Vai Thr Giy 420 425 430

Leu Gly Ala Leu Pro Leu His Ala Gln Ser Leu Val Gly Ala Asp Arg 435 440 445

Val Ser Pro Ser IIe His Lys Leu Arg Gln His Arg Pro Leu Gly Arg 450 455 460

Thr Gln Ser Ala Pro Leu Pro Gln Asn Ala Gln Ala Leu Gln His Leu 465 470 475 480

Val lle Gln Gln His Gln Gln Phe Leu Glu Lys His Lys Gln Gln 485 490 495

Phe Gin Gin Gin Leu Gin Met Asn Lys IIe IIe Pro Lys Pro Ser 500 510

Glu Pro Ala Arg Gln Pro Glu Ser His Pro Glu Glu Glu Glu Glu 515 520 525

Leu Arg Glu His Gln Ala Leu Leu Asp Glu Pro Tyr Leu Asp Arg Leu 530 540

Pro Gly Gln Lys Glu Ala His Ala Gln Ala Gly Val Gln Val Lys Gln 545 550 555 560

Glu Pro IIe Glu Ser Asp Glu Glu Glu Ala Glu Pro Pro Arg Glu Val 565 570 575

Glu Pro Gly Gln Arg Gln Pro Ser Glu Gln Glu Leu Leu Phe Arg Gln 580 585 590

Gin Ala Leu Leu Giu Gin Gin Arg Ile His Gin Leu Arg Asn Tyr 595 600 605

Gin Ala Ser Met Giu Ala Ala Giy Ile Pro Val Ser Phe Giy Giy His 610 615 620

Arg Pro Leu Ser Arg Ala Gin Ser Ser Pro Ala Ser Ala Thr Phe Pro 625 630 635 640

Val Ser Val Gin Giu Pro Pro Thr Lys Pro Arg Phe Thr Thr Giy Leu 645 650 655

Val Tyr Asp Thr Leu Met Leu Lys His Gln Cys Thr Cys Gly Ser Ser 660 665 670

Ser Ser His Pro Glu His Ala Gly Arg IIe Gln Ser IIe Trp Ser Arg 675 680 685

Leu Gin Giu Thr Giy Leu Arg Giy Lys Cys Giu Cys Ile Arg Giy Arg 690 695 700

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Leu Leu Tyr Gly Thr Asn Pro Leu Asn Arg Gln Lys Leu Asp Ser Lys 725 730 735

Lys Leu Leu Gly Ser Leu Ala Ser Val Phe Val Arg Leu Pro Cys Gly 740 745 750

Gly Val Gly Val Asp Ser Asp Thr IIe Trp Asn Glu Val His Ser Ala 755 760 765

Gly Ala Ala Arg Leu Ala Val Gly Cys Val Val Glu Leu Val Phe Lys 770 775 780

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Gly Thr Gly Pro Gly Val Gly Phe Asn Val Asn Met Ala Phe Thr Gly 885 890 895

Gly Leu Asp Pro Pro Met Gly Asp Ala Glu Tyr Leu Ala Ala Phe Arg 900 905 910

Thr Val Val Met Pro IIe Ala Ser Glu Phe Ala Pro Asp Val Val Leu 915 920 925

Val Ser Ser Gly Phe Asp Ala Val Glu Gly His Pro Thr Pro Leu Gly 930 935 940

Gly Tyr Asn Leu Ser Ala Arg Cys Phe Gly Tyr Leu Thr Lys Gln Leu 945 955 960

Met Gly Leu Ala Gly Gly Arg He Val Leu Ala Leu Glu Gly Gly His 965 970 975

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Pro Asn Ala Asn Ala Val Arg Ser Met Glu Lys Val Met Glu lle His 1010 1015 1020

Ser Lys Tyr Trp Arg Cys Leu Gin Arg Thr Thr Ser Thr Ala Gly Arg 1025 1030 1035 1040

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Pro Asp Glu Glu Pro Met Glu Glu Glu Pro Pro Leu 1075 1080

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															aag Lys	198
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															caa Gin	<b>294</b>
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									gac Asp 110							390
									ctg Leu							438
gta Vai	gca Ala	att lle 135	aac Asn	tgg Trp	tct Ser	gga Gly	ggg Gly 140	tgg Trp	cat His	cat His	gca Ala	aag Lys 145	aaa Lys	gat Asp	gaa Glu	486
									gct Ala							534
									tac Tyr							582
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Ala Leu His Lys Gin Met Arg IIe Val Lys Pro Lys Val Ala Ser Met 50 60

Glu Glu Met Ala Thr Phe His Thr Asp Ala Tyr Leu Gln His Leu Gln 65 70 75 80

Lys Val Ser Gin Glu Gly Asp Asp Asp His Pro Asp Ser ile Glu Tyr 85 90 95

Gly Leu Gly Tyr Asp Cys Pro Ala Thr Glu Gly Ile Phe Asp Tyr Ala 100 105 110

Ala Ala Ile Gly Gly Ala Thr Ile Thr Ala Ala Gln Cys Leu Ile Asp 115 120 125

Gly Met Cys Lys Val Ala IIe Asn Trp Ser Gly Gly Trp His His Ala 130 135 140

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Leu Asp Leu His His Gly Asp Gly Val Glu Asp Ala Phe Ser Phe Thr 180 185 190

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Pro Gly Thr Gly Asp Val Ser Asp Val Gly Leu Gly Lys Gly Arg Tyr 210 215 220

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Pro Met Cys Ser Phe Asn Met Thr Pro Val Gly lle Gly Lys Cys Leu 275 280 285

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Phe Thr Ala Tyr Gly Pro Asp Tyr Val Leu Glu IIe Thr Pro Ser Cys 340 345

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			cgc Arg													144	
			gaa Glu													192	
			cac His													240	
			atg Met													288	
ggt Gly	gag Glu	gac Asp	tgt Cys 100	cca Pro	gta Val	ttc Phe	gat Asp	ggc Gly 105	ctg Leu	ttt Phe	gag Glu	ttc Phe	tgt Cys 110	cag Gin	ttg Leu	336	
			ggt Gly													384	
			gct Ala													432	
			tct Ser													480	
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att He	cac His	cat His	ggt Gly 180	gac Asp	ggc G y	gtg Val	Glu	gag Glu 185	gcc Ala	ttc Phe	tac Tyr	acc Thr	acg Thr 190	gac Asp	cgg Arg	576	

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	Tyr					Gly					Ser				att alle 240	720
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		Phe										Gly			acc Thr	912
	Arg														ctg Leu 320	960
				_	aat Asn						_				Tyr	1008
					aag Lys											1056
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Arg Lys Met Glu lle Tyr Arg Pro His Lys Ala Asn Ala Glu Glu Met 50 60

Thr Lys Tyr His Ser Asp Asp Tyr IIe Lys Phe Leu Arg Ser IIe Arg 65 75 80

Pro Asp Asn Met Ser Glu Tyr Ser Lys Gln Met Gln Arg Phe Asn Val 85 90 95

Gly Glu Asp Cys Pro Val Phe Asp Gly Leu Phe Glu Phe Cys Gin Leu 100 105 110

Ser Thr Gly Gly Ser Val Ala Ser Ala Val Lys Leu Asn Lys Gin Gin 115 120 125

Thr Asp IIe Ala Val Asn Trp Ala Gly Gly Leu His His Ala Lys Lys 130 135 140

Ser Glu Ala Ser Gly Phe Cys Tyr Val Asn Asp IIe Val Leu Ala IIe 145 150 155 160

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Leu	Ala																		
〈210 〈211 〈212 〈213	) } !	1 1449 DNA Artif	icia	il															
〈220 〈221 〈222 〈223	) <   <	DS (1) Domin (HDAC	ant	nega	tive	mut	ant	(H14	OK,	H141	L) o	fhu	man	hist	one:	deac	etyl	ase-	-1
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ggg	gat	gtt	gga	aat	tac '	tat '	tat		• -	ggc	cac (		atg	-	cct		96	;	

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Artificial

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His Arg IIe Arg Met Thr His Asn Leu Leu Leu Asn Tyr Gly Leu Tyr 35 40 45

Arg Lys Met Glu lle Tyr Arg Pro His Lys Ala Asn Ala Glu Glu Met 50 55 60

Thr Lys Tyr His Ser Asp Asp Tyr IIe Lys Phe Leu Arg Ser IIe Arg 65 75 80

•	•	c	n	О

Pro Asp Asn Met Ser Glu Tyr Ser Lys Gln Met Gln Arg Phe Asn Val 85 90 95

Gly Glu Asp Cys Pro Val Phe Asp Gly Leu Phe Glu Phe Cys Gin Leu 100 105 110

Ser Thr Gly Gly Ser Val Ala Ser Ala Val Lys Leu Asn Lys Gin Gin 115 120 125

Thr Asp IIe Ala Val Asn Trp Ala Gly Gly Leu Lys Leu Ala Lys Lys 130 135 140

Ser Glu Ala Ser Gly Phe Cys Tyr Val Asn Asp Ile Val Leu Ala Ile 145 150 155 160

Leu Glu Leu Leu Lys Tyr His Gln Arg Val Leu Tyr lle Asp lle Asp 165 170 175

lle His His Gly Asp Gly Val Glu Glu Ala Phe Tyr Thr Thr Asp Arg 180 185 190

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Gly Asp Leu Arg Asp Ile Gly Ala Gly Lys Gly Lys Tyr Tyr Ala Val 210 215 220

Asn Tyr Pro Leu Arg Asp Gly IIe Asp Asp Glu Ser Tyr Glu Ala IIe 225 230 235 240

Phe Lys Pro Val Met Ser Lys Val Met Glu Met Phe Gln Pro Ser Ala 245 250 255

Val Val Leu Gin Cys Gly Ser Asp Ser Leu Ser Gly Asp Arg Leu Gly 260 265 270

Cys Phe Asn Leu Thr lie Lys Gly His Ala Lys Cys Val Glu Phe Val 275 280 285

Lys Ser Phe Asn Leu Pro Met Leu Met Leu Gly Gly Gly Tyr Thr 290 295 300

lle Arg Asn Val Ala Arg Cys Arg Thr Tyr Glu Thr Ala Val Ala Leu 305 310 320

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Phe Gly Pro Asp Phe Lys Leu His IIe Ser Pro Ser Asn Met Thr Asn 340 345 350

Gin Asn Thr Asn Giu Tyr Leu Giu Lys Ile Lys Gin Arg Leu Phe Giu 355 360 365

Asn Leu Arg Met Leu Pro His Ala Pro Gly Val Gin Met Gin Ala Ile 370 375 380

Pro	Asp	Ly:	s Arg	1 le 405		· Ile	Cys	Ser	Ser 410		Lys	Arg	; lle	415	Cys		
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Lys	Glu 450		: Asp	Pro	Glu	Glu 455	-	Lys	Glu	Val	Thr 460		Glu	Glu	Lys		
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atg Met 1	gcg Ala gat	cag Gin gtt	Thr	GIn	Gly	Thr	Arg	Arg	Lys 10 caa	Va I	Cys	Tyr	Tyr	Tyr 15 aag	Āsp	48 96	
atg Met 1 ggg Gly	gcg Ala gat Asp	cag Gin gtt Val	Thr gga Gly 20 cgc	GIn 5 aat	Gly tac Tyr	Thr tat Tyr cat	Arg tat Tyr	gga Gly 25	Lys 10 caa Gin ctg	Val ggc Gly ctc	Cys cac His	Tyr cca Pro	Tyr atg Met 30	Tyr 15 aag Lys ctc	Asp cct Pro		
atg Met 1 ggg Gly cac His	gcg Ala gat Asp cga Arg	cag Gin gtt Val atc !!e 35	Thr gga Gly 20 cgc Arg	GIN 5 aat Asn	diy tac Tyr act Thr	Thr tat Tyr cat His	tat Tyr aat Asn 40	gga Gly 25 ttg Leu	Lys 10 caa Gin ctg Leu	Val ggc Gly ctc Leu gcc	Cys cac His aac Asn	Tyr cca Pro tat Tyr 45 gct	Tyr atg Met 30 ggt Gly	Tyr 15 aag Lys ctc Leu gag	Asp cct Pro tac Tyr	96	
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		Leu										Tyr			gtt Val	672
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gag ( Glu (	gaa Glu	Glu	ttc Phe 3 420	tcc ; Ser ;	gat Asp	tct i Ser i	Glu	gag Glu 425	gag ( Glu (	gga Gly	gag Glu	ggg Gly	ggc Gly 430	cgc Arg	aag Lys	1296
ac 1	tct	tcc :	aac ·	ttc :	aaa a	aaa (	gcc a	aag	aga (	gtc	aaa	aca	gag	gat	gaa	1344

Asn Ser Ser Asn Phe Lys Lys Ala Lys Arg Val Lys Thr Glu Asp Glu 435 440 445

acc aag gag gag aag cca gaa gcc aaa ggg gtc aag gag gtc aag 1440 Thr Lys Glu Glu Lys Pro Glu Ala Lys Gly Val Lys Glu Glu Val Lys 465 470 480

ttg gcc tga 1449 Leu Ala

<210> 14 <211> 482

<212> PRT

(213) Artificial

<220>
<223> Dominant negative mutant (H199L) of human histone deacetylase-1 (HDAC1)
gene

<400> 14
Met Ala Gin Thr Gin Gly Thr Arg Arg Lys Val Cys Tyr Tyr Asp
1 5 10 15

Gly Asp Val Gly Asn Tyr Tyr Tyr Gly Gln Gly His Pro Met Lys Pro 20 25 30

His Arg IIe Arg Met Thr His Asn Leu Leu Leu Asn Tyr Gly Leu Tyr 35 40 45

Arg Lys Met Glu lle Tyr Arg Pro His Lys Ala Asn Ala Glu Glu Met 50 55 60

Thr Lys Tyr His Ser Asp Asp Tyr IIe Lys Phe Leu Arg Ser IIe Arg 65 70 75 80

Pro Asp Asn Met Ser Glu Tyr Ser Lys Gln Met Gln Arg Phe Asn Val 85 90

Gly Glu Asp Cys Pro Val Phe Asp Gly Leu Phe Glu Phe Cys Gln Leu 100 105 110

Ser Thr Gly Gly Ser Val Ala Ser Ala Val Lys Leu Asn Lys Gln Gln 115 120 125

Thr Asp IIe Ala Val Asn Trp Ala Gly Gly Leu His His Ala Lys Lys 130 135 140

Ser Glu Ala Ser Gly Phe Cys Tyr Val Asn Asp lle Val Leu Ala lle 145 150 160

Leu Glu Leu Leu Lys Tyr His Gln Arg Val Leu Tyr lle Asp lle Asp 165 170 175

lle His His Gly Asp Gly Val Glu Glu Ala Phe Tyr Thr Thr Asp Arg 180 185 190

Val Met Thr Val Ser Phe Leu Lys Tyr Gly Glu Tyr Phe Pro Gly Thr

Gly Asp Leu Arg Asp lie Gly Ala Gly Lys Gly Lys Tyr Tyr Ala Val 210 215 220

Asn Tyr Pro Leu Arg Asp Gly IIe Asp Asp Glu Ser Tyr Glu Ala IIe 225 230 235 240

Phe Lys Pro Val Met Ser Lys Val Met Glu Met Phe Gln Pro Ser Ala 245 250 255

Val Val Leu Gin Cys Giy Ser Asp Ser Leu Ser Giy Asp Arg Leu Giy 260 265 270

Cys Phe Asn Leu Thr IIe Lys Gly His Ala Lys Cys Val Glu Phe Val 275 280 285

Lys Ser Phe Asn Leu Pro Met Leu Met Leu Gly Gly Gly Tyr Thr 290 295 300

lle Arg Asn Val Ala Arg Cys Arg Thr Tyr Giu Thr Ala Val Ala Leu 305 310 315 320

Asp Thr Glu IIe Pro Asn Glu Leu Pro Tyr Asn Asp Tyr Phe Glu Tyr 325 330 335

Phe Gly Pro Asp Phe Lys Leu His IIe Ser Pro Ser Asn Met Thr Asn 340 345

Gin Asn Thr Asn Giu Tyr Leu Giu Lys IIe Lys Gin Arg Leu Phe Giu 355 360 365

Asn Leu Arg Met Leu Pro His Ala Pro Gly Val Gln Met Gln Ala IIe 370 375 380

Pro Glu Asp Ala Ile Pro Glu Glu Ser Gly Asp Glu Asp Glu Asp Asp 385 390 395 400

Pro Asp Lys Arg IIe Ser IIe Cys Ser Ser Asp Lys Arg IIe Ala Cys 405 410 415

Asn Ser Ser Asn Phe Lys Lys Ala Lys Arg Val Lys Thr Glu Asp Glu 435 440 445

Lys Glu Lys Asp Pro Glu Glu Lys Lys Glu Val Thr Glu Glu Glu Lys 450 455 460

Thr Lys Glu Glu Lys Pro Glu Ala Lys Gly Val Lys Glu Glu Val Lys 465 470 475 480

Leu Ala

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															acc Thr	96
cat His	agc Ser	ctg Leu 35	gtc Val	ctg Leu	cat His	tac Tyr	ggt Gly 40	ctc Leu	tat Tyr	aag Lys	aag Lys	atg Met 45	atc  le	gtc Val	ttc Phe	144
															gag Glu	192
									agc Ser						ggc Gly 80	240
									gta Val 90							288
ttt Phe	ccc Pro	ggg Gly	ctc Leu 100	ttt Phe	gag Glu	ttc Phe	tgc Cys	tcg Ser 105	cgt Arg	tac Tyr	aca Thr	ggc Gly	gca Ala 110	tct Ser	ctg Leu	336
									atc lle							384
									aag Lys							432
									atc ile							480
									gac Asp 170							528
									cgg Arg							576
									ggc Gly							624
									tgt Cys							672
									cac His							720
									acg Thr 250							768

													095	98		
				r Lei					, Lei				aa	c cto	c agc u Ser	816
			y Hi:					GIL					Phe		t atc n lle	864
cct Pro	cta Leu 290	Lei	gt: Va	g ctį I Lei	g ggt u Gly	ggt Gly 295	Gly	ggt	tat Tyr	act Thi	t gto Val	Arg	aat Ast	t gti n Va	t gcc I Ala	912
	Cys					ı Thr					GIL				agt Ser 320	960
					Ser					ı Tyr					ttc Phe	1008
				Asp					ile					Ser	cgc Arg	1056
cag Gin	tat Tyr	cte Leu 355	Asp	cag Gin	ato	ctc Leu	cag Gin 360	Thr	atc lle	ttt Phe	gaa Glu	aac Asn 365	Leu	aag Lys	atg Met	1104
ctg Leu	aac Asn 370	cat His	gca	cct Pro	agt Ser	gtc Val 375	Gin	att ile	cat His	gac Asp	gtg Val 380	Pro	gca	gac Asp	ctc Leu	1152
ctg Leu 385	acc Thr	tat Tyr	gac Asp	agg Arg	act Thr 390		gag Glu	gct Ala	gat Asp	gca Ala 395	Glu	gag Glu	agg Arg	ggt	cct Pro 400	1200
						cca Pro										1248
				Asp		gaa Glu						taa				1287
<210 <211 <212 <213	> 4 > F	6 128 PRT Iomo	sap	iens												
<400 Met 1		6 Lys	Thr	Val 5	Ala	Tyr	Phe	Tyr	Asp 10	Pro	Asp	Val	Gly	Asn 15	Phe	
His	Tyr	Gly	Ala 20	Gly	His	Pro	Met	Lys 25	Pro	His	Arg	Leu	Ala 30	Leu	Thr	
His	Ser	Leu 35	Val	Leu	His	Tyr	Gly 40	Leu	Tyr	Lys	Lys	Met 45	He	Val	Phe	
Lys	Pro 50	Tyr	Gin	Ala	Ser	GIn 55	His	Asp	Met	Cys	Arg 60	Phe	His	Ser	Glu	
Asp 65	Tyr	lle	Asp	Phe	Leu 70	GIn	Arg	Val	Ser	Pro 75	Thr	Asn	Met	Gln	Gly 80	
Phe	Thr	Lys	Ser	Leu 85	Asn	Ala	Phe		Va I 90	Gly	Asp	Asp	Cys	Pro 95	Val	

<b>0</b> L -	D	Clas	1	Dha	<b>61</b>	Di-	<b>^</b>	0	<b></b>	T	Thu		09598		اما
rne	Fru	шу	100	FILE	GIU	rne	Cys	105	Arg	ıyr	1111	GIY	110	361	LCL
Gin	Gly	Ala	Thr	GIn	Leu	Asn		Lys	He	Cys	Asp	lle	Ala	He	Asn

Trp Ala Gly Gly Leu His His Ala Lys Lys Phe Glu Ala Ser Gly Phe 130 135 140

Cys Tyr Val Asn Asp IIe Val IIe Gly IIe Leu Glu Leu Leu Lys Tyr 145 150 160

His Pro Arg Val Leu Tyr lle Asp lle Asp lle His His Gly Asp Gly 165 170 175

Val Gin Giu Ala Phe Tyr Leu Thr Asp Arg Val Met Thr Val Ser Phe 180 185 190

His Lys Tyr Gly Asn Tyr Phe Phe Pro Gly Thr Gly Asp Met Tyr Glu 195 200 205

Val Gly Ala Glu Ser Gly Arg Tyr Tyr Cys Leu Asn Val Pro Leu Arg 210 215 220

Asp Gly IIe Asp Asp Gln Ser Tyr Lys His Leu Phe Gln Pro Val IIe 225 230 235 240

Asn Gin Val Val Asp Phe Tyr Gin Pro Thr Cys lie Val Leu Gin Cys 245 250 255

Gly Ala Asp Ser Leu Gly Cys Asp Arg Leu Gly Cys Phe Asn Leu Ser 260 265 270

lle Arg Gly His Gly Glu Cys Val Glu Tyr Val Lys Ser Phe Asn Ile 275 280 285

Pro Leu Leu Val Leu Gly Gly Gly Gly Tyr Thr Val Arg Asn Val Ala 290 295 300

Arg Cys Trp Thr Tyr Glu Thr Ser Leu Leu Val Glu Glu Ala IIe Ser 305 310 320

Glu Glu Leu Pro Tyr Ser Glu Tyr Phe Glu Tyr Phe Ala Pro Asp Phe 325 330 335

Thr Leu His Pro Asp Val Ser Thr Arg IIe Glu Asn Gln Asn Ser Arg 340 345 350

Gin Tyr Leu Asp Gin IIe Leu Gin Thr IIe Phe Giu Asn Leu Lys Met 355 360 365

Leu Asn His Ala Pro Ser Val Gln IIe His Asp Val Pro Ala Asp Leu 370 375 380

Leu Thr Tyr Asp Arg Thr Asp Glu Ala Asp Ala Glu Glu Arg Gly Pro 385 390 395 400

Glu Glu Asn Tyr Ser Arg Pro Glu Ala Pro Asn Glu Phe Tyr Asp Gly  $405 \hspace{1cm} 410 \hspace{1cm} 415$ 

## Asp His Asp Asn Asp Lys Glu Ser Asp Val Glu IIe 420 425

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<22 <22 <22 <22	21> 22>	Dom i	. (12 nant (C3)	neg		∕e m⊔	rtant	: (H1	34K,	H13	15L)	of h	numar	his	tone	deacety lase-3
	gcc														ttc Phe	48
															acc Thr	96
	agc Ser															144
	cca Pro 50															192
	tac Tyr															240
	acc Thr															288
	ccc Pro															336
	gga Gly															384
	gct Ala 130															432
	tat Tyr															480
	cct Pro															528
	caa Gin															576
	aaa Lys					Phe										624
gtc Val	ggg Gly	gca Ala	gag Glu	agt Ser	ggc Gly	cgc Arg	tac Tyr	tac Tyr	tgt Cys	ctg Leu	aac Asn	gtg Val	ccc Pro	ctg Leu	cgg Arg	672

768

220

210

215

gat ggc att gat gac cag agt tac aag cac ctt ttc cag ccg gtt atc
Asp Gly lle Asp Asp Gln Ser Tyr Lys His Leu Phe Gln Pro Val lle
225 230 240

aac cag gta gtg gac ttc tac caa ccc acg tgc att gtg ctc cag tgt
Asn Gln Val Val Asp Phe Tyr Gln Pro Thr Cys lle Val Leu Gln Cys
250 255

gga gct gac tct ctg ggc tgt gat cga ttg ggc tgc ttt aac ctc agc
Gly Ala Asp Ser Leu Gly Cys Asp Arg Leu Gly Cys Phe Asn Leu Ser
260 265 270

atc cga ggg cat ggg gaa tgc gtt gaa tat gtc aag agc ttc aat atc
lle Arg Gly His Gly Glu Cys Val Glu Tyr Val Lys Ser Phe Asn lle
275 280 285

cct cta ctc gtg ctg ggt ggt ggt tat act gtc cga aat gtt gcc 912 Pro Leu Leu Vai Leu Giy Giy Giy Giy Tyr Thr Val Arg Asn Val Ala 290 295 300

cgc tgc tgg aca tat gag aca tcg ctg ctg gta gaa gag gcc att agt
Arg Cys Trp Thr Tyr Glu Thr Ser Leu Leu Val Glu Glu Ala lie Ser
305 310 320

gag gag ctt ccc tat agt gaa tac ttc gag tac ttt gcc cca gac ttc 1008 Glu Glu Leu Pro Tyr Ser Glu Tyr Phe Glu Tyr Phe Ala Pro Asp Phe 325 330 335

aca ctt cat cca gat gtc agc acc cgc atc gag aat cag aac tca cgc
Thr Leu His Pro Asp Val Ser Thr Arg Ile Glu Asn Gln Asn Ser Arg
340
345

cag tat ctg gac cag atc ctc cag aca atc ttt gaa aac ctg aag atg
Gin Tyr Leu Asp Gin IIe Leu Gin Thr IIe Phe Giu Asn Leu Lys Met
355 360 365

ctg aac cat gca cct agt gtc cag att cat gac gtg cct gca gac ctc
Leu Asn His Ala Pro Ser Val Gin IIe His Asp Val Pro Ala Asp Leu
370 375 380

ctg acc tat gac agg act gat gag gct gat gca gag gag agg ggt cct
Leu Thr Tyr Asp Arg Thr Asp Glu Ala Asp Ala Glu Glu Arg Gly Pro
385 390 395 400

gag gag aac tat agc agg cca gag gca ccc aat gag ttc tat gat gga 1248 Glu Glu Asn Tyr Ser Arg Pro Glu Ala Pro Asn Glu Phe Tyr Asp Gly 405 410 415

gac cat gac aat gac aag gaa agc gat gtg gag att taa 1287 Asp His Asp Asn Asp Lys Glu Ser Asp Va! Glu !!e 420 425

<210> 18 <211> 428 <212> PRT

⟨213⟩ Artificial

<220>

C223> Dominant negative mutant (H134K, H135L) of human histone deacetylase—3 (HDAC3) gene

<400> 18
Met Ala Lys Thr Val Ala Tyr Phe Tyr Asp Pro Asp Val Gly Asn Phe
1 5 10 15

His Tyr Gly Ala Gly His Pro Met Lys Pro His Arg Leu Ala Leu Thr 20 25 30

His Ser Leu Val Leu His Tyr Gly Leu Tyr Lys Lys Met Ile Val Phe 35 40 45

- Lys Pro Tyr Gln Ala Ser Gln His Asp Met Cys Arg Phe His Ser Glu 50 60
- Asp Tyr lle Asp Phe Leu Gin Arg Val Ser Pro Thr Asn Met Gin Giy 65 75 80
- Phe Thr Lys Ser Leu Asn Ala Phe Asn Val Gly Asp Asp Cys Pro Val 85 90 95
- Phe Pro Gly Leu Phe Glu Phe Cys Ser Arg Tyr Thr Gly Ala Ser Leu 100 105 110
- Gin Gly Ala Thr Gin Leu Asn Asn Lys IIe Cys Asp IIe Ala IIe Asn 115 120 125
- Trp Ala Gly Gly Leu Lys Leu Ala Lys Lys Phe Glu Ala Ser Gly Phe 130 135 140
- Cys Tyr Val Asn Asp lie Val lie Gly lie Leu Glu Leu Leu Lys Tyr 145 150 155 160
- His Pro Arg Val Leu Tyr lle Asp lle Asp lle His His Gly Asp Gly 165 170 175
- Val Gin Giu Ala Phe Tyr Leu Thr Asp Arg Vai Met Thr Val Ser Phe 180 185 190
- His Lys Tyr Gly Asn Tyr Phe Phe Pro Gly Thr Gly Asp Met Tyr Glu 195 200 205
- Val Gly Ala Glu Ser Gly Arg Tyr Tyr Cys Leu Asn Val Pro Leu Arg 210 215 220
- Asp Gly IIe Asp Asp Gln Ser Tyr Lys His Leu Phe Gln Pro Val IIe 225 230 235 240
- Asn Gin Val Val Asp Phe Tyr Gin Pro Thr Cys IIe Val Leu Gin Cys 245 250 250
- Gly Ala Asp Ser Leu Gly Cys Asp Arg Leu Gly Cys Phe Asn Leu Ser 260 265 270
- lle Arg Gly His Gly Glu Cys Val Glu Tyr Val Lys Ser Phe Asn lle 275 285
- Pro Leu Leu Val Leu Gly Gly Gly Gly Tyr Thr Val Arg Asn Val Ala 290 295 300
- Arg Cys Trp Thr Tyr Glu Thr Ser Leu Leu Val Glu Glu Ala IIe Ser 305 310 315 320
- Glu Glu Leu Pro Tyr Ser Glu Tyr Phe Glu Tyr Phe Ala Pro Asp Phe 325 330 335
- Thr Leu His Pro Asp Val Ser Thr Arg lle Glu Asn Gln Asn Ser Arg

Gin Tyr Leu Asp Gin IIe Leu Gin Thr IIe Phe Giu Asn Leu Lys Met 355 360 365

Leu Asn His Ala Pro Ser Val Gln IIe His Asp Val Pro Ala Asp Leu 370 375 380

Leu Thr Tyr Asp Arg Thr Asp Glu Ala Asp Ala Glu Glu Arg Gly Pro 385 390 395

Glu Glu Asn Tyr Ser Arg Pro Glu Ala Pro Asn Glu Phe Tyr Asp Gly 405 410 415

Asp His Asp Asn Asp Lys Glu Ser Asp Val Glu Ile 420 425

⟨210⟩ 19
(211) 1287 (212) DNA (213) Artificial
<220> <221> CDS
<222> (1) (1287) <223> Dominant negative mutant (H193L) of human histone deacetylase-3 (HDAC3) gene
<400> 19 atg gcc aag acc gtg gcc tat ttc tac gac ccc gac gtg ggc aac ttc 48
Met Ala Lys Thr Val Ala Tyr Phe Tyr Asp Pro Asp Val Gly Asn Phe 1 5 10 15
cac tac gga gct gga cac cct atg aag ccc cat cgc ctg gca ttg acc His Tyr Gly Ala Gly His Pro Met Lys Pro His Arg Leu Ala Leu Thr 20 25 30
cat agc ctg gtc ctg cat tac ggt ctc tat aag aag atg atc gtc ttc His Ser Leu Val Leu His Tyr Gly Leu Tyr Lys Lys Met Ile Val Phe 35 40 45
aag cca tac cag gcc tcc caa cat gac atg tgc cgc ttc cac tcc gag Lys Pro Tyr Gln Ala Ser Gln His Asp Met Cys Arg Phe His Ser Glu 50 55 60
gac tac att gac ttc ctg cag aga gtc agc ccc acc aat atg caa ggc Asp Tyr lle Asp Phe Leu Gin Arg Vai Ser Pro Thr Asn Met Gin Gly 65 70 75 80
ttc acc aag agt ctt aat gcc ttc aac gta ggc gat gac tgc cca gtg Phe Thr Lys Ser Leu Asn Ala Phe Asn Val Gly Asp Asp Cys Pro Val 85 90 95
ttt ccc ggg ctc ttt gag ttc tgc tcg cgt tac aca ggc gca tct ctg Phe Pro Gly Leu Phe Glu Phe Cys Ser Arg Tyr Thr Gly Ala Ser Leu 100 105 110
Gin Giy Ala Thr Gin Leu Asn Asn Lys IIe Cys Asp IIe Ala IIe Asn 115 120 125
tgg gct ggt ggt ctg cac cat gcc aag aag ttt gag gcc tct ggc ttc Trp Ala Gly Gly Leu His His Ala Lys Lys Phe Glu Ala Ser Gly Phe 130 135 140
tgc tat gtc aac gac att gtg att ggc atc ctg gag ctg ctc aag tac Cys Tyr Val Asn Asp lie Val lie Gly lie Leu Glu Leu Leu Lys Tyr 145 150 155 160

													0959	R		
cac His	cct Pro	cgg Arg	gtg Val	ctc Leu 165	Tyr	att	gac Asp	att	gac Asp 170	He	cac His	cat	ggt	gac	ggg Gly	528
				Phe					Arg			acg Thr		Ser	ttc Phe	576
ctt Leu	aaa Lys	tac Tyr 195	Gly	aat Asn	tac Tyr	ttc Phe	ttc Phe 200	cct Pro	ggc Gly	aca Thr	ggt Gly	gac Asp 205	atg Met	tat Tyr	gaa Glu	624
		Ala										gtg Val				672
gat Asp 225	Gly	att lle	gat Asp	gac Asp	cag Gin 230	agt Ser	tac Tyr	aag Lys	cac His	ctt Leu 235	ttc Phe	cag Gin	ccg Pro	gtt Val	atc 11e 240	720
												gtg Val				768
gga Gly	gct Ala	gac Asp	tct Ser 260	ctg Leu	ggc Gly	tgt Cys	gat Asp	cga Arg 265	ttg Leu	ggc Gly	tgc Cys	ttt Phe	aac Asn 270	ctc Leu	agc Ser	816
atc Ile	cga Arg	ggg Gly 275	cat His	ggg Gly	gaa Glu	tgc Cys	gtt Val 280	gaa Glu	tat Tyr	gtc Val	aag Lys	agc Ser 285	ttc Phe	aat Asn	atc lle	864
cct Pro	cta Leu 290	ctc Leu	gtg Val	ctg Leu	ggt Gly	ggt Gly 295	ggt Gly	ggt Gly	tat Tyr	act Thr	gtc Val 300	cga Arg	aat Asn	gtt Vai	gcc Ala	912
cgc Arg 305	tgc Cys	tgg Trp	aca Thr	tat Tyr	gag Glu 310	aca Thr	tcg Ser	ctg Leu	ctg Leu	gta Val 315	gaa Glu	gag Glu	gcc Ala	att   e	agt Ser 320	960
												gcc Ala				1008
												cag Gin				1056
												aac Asn 365				1104
												cct Pro				1152
ctg Leu 385	acc Thr	tat Tyr	gac Asp	agg Arg	act Thr 390	gat Asp	gag Glu	gct Ala	Asp	gca Ala 395	gag Glu	gag Glu	agg Arg	ggt Gly	cct Pro 400	1200
			Tyr									ttc Phe	Tyr			12 <b>4</b> 8
			aat Asn 420				Ser					taa				1287

<210> 20
<211> 428
<212> PRT
<213> Artificial

<220>

<223> Dominant negative mutant (H193L) of human histone deacetylase-3 (HDAC3) gene

<400> 20
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1 5 10 15

His Tyr Gly Ala Gly His Pro Met Lys Pro His Arg Leu Ala Leu Thr 20 30

His Ser Leu Val Leu His Tyr Gly Leu Tyr Lys Lys Met IIe Val Phe 35 40 45

Lys Pro Tyr Gln Ala Ser Gln His Asp Met Cys Arg Phe His Ser Glu 50 60

Asp Tyr lie Asp Phe Leu Gin Arg Val Ser Pro Thr Asn Met Gin Giy 65 75 80

Phe Thr Lys Ser Leu Asn Ala Phe Asn Val Gly Asp Asp Cys Pro Val 85 90 95

Phe Pro Gly Leu Phe Glu Phe Cys Ser Arg Tyr Thr Gly Ala Ser Leu 100 105 110

Gin Gly Ala Thr Gin Leu Asn Asn Lys IIe Cys Asp IIe Ala IIe Asn 115 120 125

Trp Ala Gly Gly Leu His His Ala Lys Lys Phe Glu Ala Ser Gly Phe 130 135 140

Cys Tyr Val Asn Asp IIe Val IIe Gly IIe Leu Glu Leu Leu Lys Tyr 145 150 160

His Pro Arg Val Leu Tyr lle Asp lle Asp lle His His Gly Asp Gly 165 170 175

Val Gin Giu Ala Phe Tyr Leu Thr Asp Arg Val Met Thr Val Ser Phe 180 185 190

Leu Lys Tyr Gly Asn Tyr Phe Phe Pro Gly Thr Gly Asp Met Tyr Glu 195 200 205

Val Gly Ala Glu Ser Gly Arg Tyr Tyr Cys Leu Asn Val Pro Leu Arg 210 215 220

Asp Gly IIe Asp Asp Gin Ser Tyr Lys His Leu Phe Gin Pro Val IIe 225 230 235 240

Asn Gln Val Val Asp Phe Tyr Gln Pro Thr Cys IIe Val Leu Gln Cys 245 250 255

Gly Ala Asp Ser Leu Gly Cys Asp Arg Leu Gly Cys Phe Asn Leu Ser 260 265 270

lle Arg Gly His Gly Glu Cys Val Glu Tyr Val Lys Ser Phe Asn Ile 275 280 285

Pro	290		, vai	Leu	luiy	295		GII Y	ıyr	ınr	300		, ASI	ı va	Ala	
Arg 305		Trp	Thr	Tyr	Glu 310		Ser	Leu	Leu	Va I 315		Glu	Ala	ılle	Ser 320	
Glu	Glu	ı Leu	ı Pro	Tyr 325		Glu	Tyr	Phe	G1u 330		Phe	Ala	Pro	Asp 335	Phe	
Thr	Leu	ı His	Pro 340		Val	Ser	Thr	Arg 345		Glu	Asn	Gin	Asn 350		Arg	
GIn	Tyr	Leu 355		GIn	lle	Leu	Gin 360		He	Phe	Glu	Asn 365		Lys	Met	
Leu	Asr 370		Ala	Pro	Ser	Val 375		lle	His	Asp	Val 380		Ala	Asp	Leu	
Leu 385		Tyr	Asp	Arg	Thr 390		Glu	Ala	Asp	Ala 395		Glu	Arg	Gly	Pro 400	
Glu	Glu	Asn	Tyr	Ser 405	Arg	Pro	Glu	Ala	Pro 410	Asn	Glu	Phe	Tyr	Asp 415		
Asp	His	Asp	Asn 420		Lys	Glu	Ser	Asp 425	Val	Glu	lle					
<210 <211 <212 <213	!> ?>	21 1458 DNA Homo	sap	iens												
<220 <221 <222 <223	) }		. (14! n <b>N</b> —(		(RD3)	ger	ne									
<400 gaa Glu 1	gtc	21 ctt Leu	cag Gin	cct Pro 5	gct Ala	cca Pro	cat His	caa Gin	gtg Val 10	ata   e	act Thr	aat Asn	ctc Leu	cct Pro 15	gaa Glu	48
					aca Thr											96
					acc Thr											144
Met					tca Ser											192
	Asn				tac Tyr <b>7</b> 0											240
tct Ser																288
act Thr																336

			Glu					Arg					Gly		gtc Val	384
		Thr					Gin					Thr			act Thr	432
	Thr					Vai					Ser				tct Ser 160	480
					Pro					Thr					gag Glu	528
				Gly					Met					Ser	agt Ser	576
			Gly					Ala	tcc Ser				Val		tat Tyr	624
		Lys							tat Tyr			He				672
									gct Ala							720
									ata Ile 250						Met	768
agg Arg	gag Glu	tct Ser	cct Pro 260	gta Val	tca Ser	gca Ala	ccg Pro	tta Leu 265	gag Glu	ggg Gly	ctg Leu	ata ile	tgc Cys 270	cga Arg	gca Ala	816
									ctc Leu							864
									aga Arg							912
Ξ.	_								att Ile				_			960
									aaa Lys 330							1008
									tcc Ser							1056
						Glu			aaa Lys							1104
Ser					Пe				att lie	Ser						1152
				Asn					gcc Ala							1200
									tcc Ser			Met				1248

415

	405		410	415
Glu lle Val P	ca gag aac ro Glu Asn 20	ata aaa gtg lle Lys Val 425	gta gaa cgg Val Glu Arg	gga aaa tat gag Gly Lys Tyr Glu 430
gat gtg aaa g Asp Val Lys A 435	ca ggc gag la Gly Glu	acc gtg cgt Thr Val Arg 440	Ser Arg His	acg tca gtg gta Thr Ser Val Val 445
	ro Ser Val			gaa gct ccc aaa Glu Ala Pro Lys
gca caa ctg a Ala Gin Leu S 465	gc cct ggg er Pro Gly 470	att tat gat lle Tyr Asp	gac acc agt Asp Thr Ser 475	gca cgg agg acc Ala Arg Arg Thr 480
cct gtg agt t Pro Val Ser T				
<210> 22 <211> 486 <212> PRT <213> Homo s:	apiens			
<400> 22 Glu Val Leu G 1	in Pro Ala i 5		Val lie Thr / 10	Asn Leu Pro Glu 15
Gly Val Arg Lo		Thr Arg Pro 25	Thr Arg Pro I	Pro Pro Leu 30
lle Pro Ser Se 35	er Lys Thr	Thr Val Ala S 40		Pro Ser Phe Ile 15
Met Gly Gly Se 50		Gin Gly Thr 8 55	Pro Gly Thr 1 60	yr Leu Thr Ser
His Asn Gln Al 65	a Ser Tyr 1 70	Thr Gin Giu 1	Thr Pro Lys F 75	Pro Ser Val Gly 80
Ser lie Ser Le	eu Gly Leu F 85		iin Glu Ser A 10	ala Lys Ser Ala 95
Thr Leu Pro Ty 10		Sin Glu Glu F 105	he Ser Pro A	rg Ser Gin Asn 110
Ser Gin Pro Gi 115	u Gly Leu L	eu Val Arg A 120		lu Gly Val Val 25
Arg Gly Thr Al 130	· · · · · · · · · · · · · · · · · · ·	le Gin Giu 6 35	ily Ser Ile T 140	hr Arg Gly Thr
Pro Thr Ser Ly 145	s lle Ser V 150	al Glu Ser I	le Pro Ser L 155	eu Arg Gly Ser 160
lle Thr Gin Gi	y Thr Pro A 165		in Thr Gly I 70	le Pro Thr Glu 175
Ala Leu Val Ly 18		le Ser Arg M 185	et Pro lle G	lu Asp Ser Ser 190

- Pro Glu Lys Gly Arg Glu Glu Ala Ala Ser Lys Gly His Val IIe Tyr 195 200 205
- Glu Gly Lys Ser Gly His IIe Leu Ser Tyr Asp Asn IIe Lys Asn Ala 210 215 220
- Arg Glu Gly Thr Arg Ser Pro Arg Thr Ala His Glu IIe Ser Leu Lys 225 230 235 240
- Arg Ser Tyr Glu Ser Val Glu Gly Asn Ile Lys Gln Gly Met Ser Met 245 250 250
- Arg Glu Ser Pro Val Ser Ala Pro Leu Glu Gly Leu lle Cys Arg Ala 260 265 270
- Leu Pro Arg Gly Ser Pro His Ser Asp Leu Lys Glu Arg Thr Val Leu 275 280 285
- Ser Gly Ser lie Met Gin Gly Thr Pro Arg Ala Thr Thr Glu Ser Phe 290 295 300
- Glu Asp Gly Leu Lys Tyr Pro Lys Gin IIe Lys Arg Glu Ser Pro Pro 305 310 315 320
- lle Arg Ala Phe Glu Gly Ala lle Thr Lys Gly Lys Pro Tyr Asp Gly 325 330 335
- lle Thr Thr lle Lys Glu Met Gly Arg Ser lle His Glu lle Pro Arg 340 345 350
- Gin Asp IIe Leu Thr Gin Glu Ser Arg Lys Thr Pro Glu Vai Vai Gin 355 360 365
- Ser Thr Arg Pro IIe IIe Glu Gly Ser IIe Ser Gln Gly Thr Pro IIe 370 375 380
- Lys Phe Asp Asn Asn Ser Gly Gln Ser Ala lie Lys His Asn Val Lys 385 400
- Ser Leu lie Thr Gly Pro Ser Lys Leu Ser Arg Gly Met Pro Pro Leu 405 410 415
- Glu lie Vai Pro Glu Asn lie Lys Vai Vai Glu Arg Gly Lys Tyr Glu 420 425 430
- Asp Val Lys Ala Gly Glu Thr Val Arg Ser Arg His Thr Ser Val Val 435 440 445
- Ser Ser Gly Pro Ser Val Leu Arg Ser Thr Leu His Glu Ala Pro Lys 450 455 460
- Ala Gin Leu Ser Pro Gly IIe Tyr Asp Asp Thr Ser Ala Arg Arg Thr 465 470 475 480
- Pro Val Ser Tyr Gin Asn

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        23
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        731
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 <213>
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      5'-flanking region of Human interleukin-2 (IL-2) gene
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 agatatataa toattttaaa ttaaaatago gttaaacagt acctcaagot caataagoat
                                                                        120
tttaagtatt ctaatcttag tatttctcta gctgacatgt aagaagcaat ctatcttatt
                                                                        180
                                                                        240
gtatgcaatt agctcattgt gtggataaaa aggtaaaacc attctgaaac aggaaaccaa
                                                                        300
tacacttcct gtttaatcaa caaatctaaa catttattct tttcatctgt ttactcttgc
tcttgtccac cacaatatgc tattcacatg ttcagtgtag ttttaggaca aagaaaattt
                                                                        360
totgagttac ttttgtatcc ccacccctt aaagaaagga ggaaaaactg tttcatacag
                                                                       420
aaggogttaa ttgcatgaat tagagctatc acctaagtgt gggctaatgt aacaaagagg
                                                                        480
gatttcacct acatccattc agtcagtctt tgggggttta aagaaattcc aaagagtcat
                                                                        540
cagaagagga aaaatgaagg taatgttttt tcagacaggt aaagtctttg aaaatatgtg
                                                                        600
taatatgtaa aacattttga cacccccata atatttttcc agaattaaca gtataaattg
                                                                        660
                                                                        720
catctcttgt tcaagagttc cctatcactc tctttaatca ctactcacag taacctcaac
                                                                        731
tcctgccaca a
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       24
       527
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(212)
       DNA
<213>
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      (73).. (506)
5'-flanking region of Human interleukin-2 (IL-2) gene
<222>
〈223〉
gggnnnnnng gngatcctct accactatag ggcgaattga atttagcggc cgcganttcg
                                                                         60
cccttcgcta gctgctcttg tccaccacaa tatgctattc acatgttcag tgtagtttta
                                                                        120
                                                                       180
ggacaaagaa aattttctga gttacttttg tatccccacc cccttaaaga aaggaggaaa
aactgtttca tacagaaggc gttaattgca tgaattagag ctatcaccta agtgtgggct
                                                                       240
                                                                       300
aatgtaacaa agagggattt cacctacatc cattcagtca gtctttgggg gtttaaagaa
attocaaaga gtoatoagaa gaggaaaaat gaaggtaatg ttttttoaga caggtaaagt
                                                                       360
ctttgaaaat atgtgtaata tgtaaaacat tttgacaccc ccataatatt tttccagaat
                                                                       420
taacagtata aattgcatct cttgttcaag agttccctat cactctcttt aatcactact
                                                                       480
                                                                       527
cacagtaacc tcaactcctg ccacaagctt cgaagggcga attcgtt
⟨210⟩
      25
      900
〈211〉
      DNA
<213>
      Homo sapiens
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<400> 25	
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ctggctccca cctcagtttc ccgcctccaa ggcagcatgg cgggcaagaa gttgaggcca	120
etgtecetgg gtgtteetae ecceaeace teaececaag acageetgtt actgeggege	180
caacagccac ggtcgcctac atctgataag acttatctgc tgccccaggg caggccggag	240
ctggcgtaag ccccagtggg gcgctaagtg agtgtgcccc tgcctcccgc cagcactggc	300
ctggcctgca ggcttagcct gggtcatcaa ggtatcccac aggctctagt tcaaatccag	360
cagaacctct ctgagcctca ctcttctcac ctgcaaaatg ggtacagcca catcccttct	420
ctccctgcag ccaggaagac gcacatacac aggagtctag cccacaccgg ccccgcacaa	480
attaaggget ttactetetg aaaageecag tgaagteatg aaaceatate tgetatttte	540
atttatcttg gtttcagcct attttgcttg tctggacact acagtccacg ggagcctagg	600
togagogagg tocaagaato cocagggtgg goagggaggg tggaagaggg cotocagtgo	660
ccaagaggtg ccccacaagc atgggacccg ccccctccc tggactgccc cacccactgg	720
ggcaccagcc actccctggg gaggagggag gagggagaag ggagggaggg agggagggag	780
gaagggagcc tcaaaggcca aggccagcca ggacaccccc tgggatcaca ctgagcttgc	840
cacatececa aggeggeega acceteegea accaceaaag ettataaggg egaattegtt	900
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<213> Homo sapiens	
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<222> (11) (647) <223> Promoter region of Human GATA-1 gene	
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aagagaggac attgaagaag agtctcaaac ttaggcctga cggagaagac gcgcggccag	120
gacaccccac ccccgccctc gtctccccca aagcctgatc tggccccact gattccctta	180
totgoccact cocagctgoc toottgotgg ctgaactgte geogragact totgageetg	240
cgcccctcc acggggatgg gggagggaat ggggtgaggc ctggcctcac agcctcgggg	300
tttccagctc ttgctggagg cagggctctg gggcgcccta ctcctcaccc ttggcttctc	360
ttcctgagcg ctctgtgctc tccagaaatg aagaaatggg gtgagtccag cggccaaacc	420
cttgtcttag ctcttagaca tgcctcgagc ctgccattcc ctgtgaggac agatttccct	480
atgttgcgac cgctgcttct aataataata atgatgatga taattcccat ttacagagca	540
caccatttat ggtgtgccag caggccctgt gctgagtggt tcctacccac gtggggggct	600
aggactttac ccgttttcca gatgaagaaa ctgaggctca gagggcgcta gcataagggc	660
⟨210⟩ 27	
(211) 32 (212) DNA	
No. 1 Aug. 10 (1971)	

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<213> Artificial
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 〈223〉
        PCR primer for amplifying the 5'-flanking region of Human interleukin-2
         (IL-2) gene
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                                                                         32
 <210> 28
 <211>
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       DNA
 <213>
       Artificial
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 <223>
        PCR primer for amplifying the 5'-flanking region of Human interleukin-2
 <400> 28
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                                                                         30
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 <212>
        DNA
 <213> Homo sapiens
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⟨222⟩ (1).. (777)
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        Corresponding to the sequence (+661 to +1437) in the GenBank database
        (Acession: HSIL05)
<400> 29
atcagtatcc ttgaatcgaa acctttttct gagtatttaa caatcgcacc ctttaaaaaa
                                                                        60
tgtacataga cattaagaga cttaaacaga tatataatca ttttaaatta aaatagcgtt
                                                                       120
aaacagtacc tcaagctcaa taagcatttt aagtattcta atcttagtat ttctctagct
                                                                       180
gacatgtaag aagcaatcta tottattgta tgcaattagc totttgtgtg gataaaaagg
                                                                       240
taaaaccatt ctgaaacagg aaaccaatac acttcctgtt taatcaacaa atctaaacat
                                                                       300
ttattetttt catetgttta etettgetet tgtecaccae aatatgetat teacatgtte
                                                                       360
agtgtagttt tatgacaaag aaaattttct gagttacttt tgtatcccca cccccttaaa
                                                                       420
gaaaggagga aaaactgttt catacagaag gcgttaattg catgaattag agctatcacc
                                                                       480
taagtgtggg ctaatgtaac aaagagggat ttcacctaca tccattcagt cagtctttgg
                                                                       540
gggtttaaag aaattccaaa gagtcatcag aagaggaaaa atgaaggtaa tgttttttca
                                                                       600
gactggtaaa gtotttgaaa atatgtgtaa tatgtaaaac attttgacac occcataata
                                                                       660
tttttccaga attaacagta taaattgcat ctcttgttca agagttccct atcactcttt
                                                                       720
aatcactact cacagtaacc tcaactcctg ccacaatgta caggatgcaa ctcctgt
                                                                       777
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<213>
      Artificial
<220>
<223>
       PCR primer for amplifying the 5'-flanking region of Human interleukin-2
       (IL-2) gene
<400> 30
cgctagctgc tcttgtccac cacaatatgc
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<210>
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        DNA
 〈212〉
        Homo sapiens
 <213>
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        misc_feature
(1)..(538)
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        Corresponding to the sequence (+901 to +1438) in the GenBank database
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        (Acession: HSIL05)
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 taaaaccatt ctgaaacagg aaaccaatac acttcctgtt taatcaacaa atctaaacat
ttattctttt catctgttta ctcttgctct tgtccaccac aatatgctat tcacatgttc
                                                                       120
agtgtagttt tatgacaaag aaaattttct gagttacttt tgtatcccca cccccttaaa
                                                                       180
gaaaggagga aaaactgttt catacagaag gcgttaattg catgaattag agctatcacc
                                                                       240
taagtgtggg ctaatgtaac aaagagggat ttcacctaca tccattcagt cagtctttgg
                                                                       300
                                                                       360
gggtttaaag aaattccaaa gagtcatcag aagaggaaaa atgaaggtaa tgttttttca
gactggtaaa gtctttgaaa atatgtgtaa tatgtaaaac attttgacac ccccataata
                                                                       420
tttttccaga attaacagta taaattgcat ctcttgttca agagttccct atcactcttt
                                                                       480
aatcactact cacagtaacc tcaactcctg ccacaatgta caggatgcaa ctcctgtc
                                                                       538
<210>
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〈211〉
       28
⟨212⟩
       DNA
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      Artificial
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<400> 32
atagatotat cootggotoc cacotoag
                                                                        28
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       33
<211>
       28
<212>
       DNA
<213>
       Artificial
〈220〉
<223>
       PCR primer for amplifying the promoter region of Human GATA-1 gene
<400> 33
ataagctttg gtggttgcgg agggttcg
                                                                       28
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(211)
      28
(212)
      DNA
<213> Artificial
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<223> PCR primer for amplifying the promoter region of Human GATA-1 gene
<400> 34
atggtaccac cccagaagat gccaggag
                                                                       28
<210>
      35
<211>
      28
<212>
      DNA
<213>
      Artificial
<220>
<223> PCR primer for amplifying the promoter region of Human GATA-1 gene
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<400> 35
                                                                         28
 atgctagcgc cctctgagcc tcagtttc
 <210>
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        23
 <212> DNA
 <213> Artificial
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<223> PCR primer for amplifying a human histone deacetylase-1 (HDAC1) gene
<400> 36
                                                                        23
gaggaattca agatggcgca gac
<210> 37
<211> 25
<212> DNA
⟨213⟩ Artificial
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<223> PCR primer for amplifying a human histone deacetylase-1 (HDAC1) gene
<400> 37
ggagcggccg cttcaggcca acttg
                                                                        25
<210> 38
<211> 24
<212> DNA
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<223> PCR primer for amplifying a human histone deacetylase-2 (HDAC2) gene
<400> 38
ggggatccat ggcgtacagt caag
                                                                        24
<210> 39
<211> 29
<212> DNA
<213> Artificial
<223> PCR primer for amplifying a human histone deacetylase-2 (HDAC2) gene
<400> 39
ggtgcggccg ccaaattcag gggttgctg
<210> 40
<211> 22
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(213) Artificial
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<223> PCR primer for amplifying a human histone deacetylase-3 (HDAC3) gene
<400> 40
                                                                       22
ccggatccac catggccaag ac
<210> 41
<211> 28
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<400> 41
gcagcggccg ccactcttaa atctccac
                                                                       28
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<210>
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        28
 〈212〉
       DNA
        Artificial
 <213>
 (223) PCR primer for amplifying a human histone deacetylase-4 (HDAC4) gene
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                                                                       28
 <210> 43
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 <220>
 <223> PCR primer for amplifying a human histone deacetylase-4 (HDAC4) gene
 <400> 43
 aaggogoogo agottogagg gagtgotac
                                                                       29
 <210> 44
 <211> 27
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<400> 44
ggcaagctta tgaactctcc caacgag
                                                                       27
<210> 45
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<212> DNA
<213> Artificial
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<223> PCR primer for amplifying a human histone deacetylase-5 (HDAC5) gene
<400> 45
gggcggccgc gtcacagggc aggctcctg
                                                                       29
<210> 46
<211> 27
<212> DNA
<213> Artificial
(223) PCR primer for amplifying a human histone deacetylase-6 (HDAC6) gene
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gcgaagctta tgacctcaac cggccag
                                                                      27
<210>
      47
〈211〉
      33
(212) DNA
(213) Artificial
<220>
<223> PCR primer for amplifying a human histone deacetylase-6 (HDAC6) gene
gcatgcggcc gcttagtgtg ggtggggcat atc
                                                                      33
<210> 48
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<211> 26
 <212>
       DNA
 <213>
       Artificial
 <220>
 <223> PCR primer for amplifying a human histone deacetylase-7 (HDAC7) gene
 <400> 48
cgaattcagc cgcagcccat ggacct
                                                                       26
 <210> 49
 <211>
      26
 <212> DNA
<213> Artificial
 <220>
<223> PCR primer for amplifying a human histone deacetylase-7 (HDAC7) gene
<400> 49
cggtaccctg tgcacccgga tcacgg
                                                                       26
<210> 50
<211>
       26
 <212> DNA
<213> Artificial
<220>
<223> PCR primer for amplifying a human histone deacetylase-8 (HDAC8) gene
<400> 50
cgaattcttt aagcggaaga tggagg
                                                                       26
<210> 51
<211> 26
<212>
      DNA
<213> Artificial
<220>
<223> PCR primer for amplifying a human histone deacetylase-8 (HDAC8) gene
<400> 51
                                                                       26
aggtaccgac cacatgcttc agattc
⟨210⟩
       52
〈211〉
       24
<212> DNA
₹213>
      Artificial
<220>
<223> PCR primer for amplifying a human histone deacetylase-3 (HDAC3) gene
<400> 52
ctgaattcac catggccaag accg
                                                                      24
<210> 53
<211> 61
<212> DN
      DNA
<213>
      Artificial
<220>
<223> PCR primer for adding a Flag sequence to a human histone deacety!ase-3
       (HDAC3) gene
gggcggccgc ctacttgtca tcgtcgtcct tgtaatcggt accaatctcc acatcgcttt
                                                                      60
C
                                                                      61
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<210> 54

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<211> 8
<212> PRT
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1
5
 <210>
        55
 ⟨211⟩ 31
 <212> DNA
 ⟨213⟩ Artificial
 <220>
 ⟨223⟩
       PCR primer for adding a Kpn I site to a human histone deacetylase-1
        (HDAC1) gene
 <400> 55
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                                                                            31
 <210> 56
 <211>
       29
 <212>
       DNA
 ⟨213⟩ Artificial
 <220>
 <223>
        PCR primer for adding a Kpn I site to a human histone deacetylase-2
        (HDAC2) gene
<400> 56
atcggtaccg gggttgctga gctgttctg
                                                                            29
<210> 57
<211> 27
<212> DNA
<213> Artificial
<220>
<223>
       PCR primer for adding a Bgl II site to a human histone deacetylase-4
        (HDAC4) gene
<400> 57
                                                                           27
gatagatoto aggggcggct cototto
<210> 58
<211> 46
<212> DNA
<213> Artificial
(223) Nucleotide sequence having a Flag nucleotide sequence
<400> 58
aattootgoa gagatotgat tacaaggacg acgatgacaa gtaggo
                                                                           46
<210> 59
<211> 46
<212> DNA
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<220>
(223) Nucleotide sequence having a Flag nucleotide sequence
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<210>
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        DNA
 <213> Artificial
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        PCR primer for creating a dominant negative mutant (H802K, H803L) of human
 <223>
        histone deacetylase-4 (HDAC4) gene
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        20
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(213) Artificial
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<223> PCR primer for creating a dominant negative mutant (H802K, H803L) of human histone deacetylase-4 (HDAC4) gene
<400> 61
                                                                                20
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<212>
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        20
        DNA
        Artificial
<213>
<220>
       PCR primer for creating a dominant negative mutant (H802K, H803L) of human histone deacetylase-4 (HDAC4) gene
<223>
<400> 62
                                                                               20
cccctggaa agcttgcgga
<210> 63
<211>
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       DNA
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      Artificial
<220>
       PCR primer for creating a dominant negative mutant (H802K, H803L) of human histone deacetylase-4 (HDAC4) gene
<223>
<400> 63
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<212> DNA
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<220>
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       PCR primer for creating a dominant negative mutant (H863L) of human
       histone deacetylase-4 (HDAC4) gene
<400> 64
cctgtacatg tccctccttc g
                                                                               21
<210>
       65
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       20
       DNA
       Artificial
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       histone deacetylase-4 (HDAC4) gene
<400>
       65
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C223> PCR primer for creating a dominant negative mutant (H199L) of human histone deacetylase-1 (HDAC1) gene

**<400> 70** 

gacggcgtgg aagaggcctt c

21

<210> 71 <211> 26

<212> DNA

<213> Artificial

<220>

<223> PCR primer for creating a dominant negative mutant (H199L) of human

histone deacetylase-1 (HDAC1) gene

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<400> 71
                                                                                  26
 gaagtactct ccatacttaa gaaagg
 <210> 72
 <211> 26
 <212> DNA
 ⟨213⟩ Artificial
        PCR primer for creating a dominant negative mutant (H199L) of human histone deacetylase-1 (HDAC1) gene
 ⟨223⟩
<400> 72
ctgtgtcctt tcttaagtat ggagag
                                                                                  26
<210> 73
<211> 22
 <212> DNA
<213> Artificial
<220>
        PCR primer for creating a dominant negative mutant (H199L) of human histone deacetylase-1 (HDAC1) gene
<223>
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                                                                                  22
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<210> 74
<211> 23
 <212> DNA
<213>
       Artificial
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        PCR primer for creating a dominant negative mutant (H134K, H135L) of human
<223>
        histone deacetylase-3 (HDAC3) gene
<400> 74
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aacccagctg aacaacaaga tctg
<210>
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        75
        26
<212> DNA
<213> Artificial
<220>
<223>
       PCR primer for creating a dominant negative mutant (H134K, H135L) of human histone deacetylase-3 (HDAC3) gene
<400> 75
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ctcaaacttc ttggcaagct tcagac
<210> 76
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      25
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(213) Artificial
<220>
       PCR primer for creating a dominant negative mutant (H134K, H135L) of human histone deacetylase-3 (HDAC3) gene
<223>
<400> 76
                                                                                 25
tggtggtctg aagcttgcca agaag
<210> 77
<211>
      21
(212)
      DNA
(213) Artificial
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〈220〉
 <223>
        PCR primer for creating a dominant negative mutant (H134K, H135L) of human
         histone deacetylase-3 (HDAC3) gene
 <400> 77
 cccgtcacca tggtggatgt c
                                                                                21
 <210> 78
 <211>
        23
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        DNA
 ⟨213⟩
        Artificial
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        PCR primer for creating a dominant negative mutant (H193L) of human histone deacetylase-3 (HDAC3) gene
 <223>
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                                                                               23
<210> 79
<211> 26
 <212> DNA
 <213>
       Artificial
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<223>
        PCR primer for creating a dominant negative mutant (H193L) of human
        histone deacetylase-3 (HDAC3) gene
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gaagtaattt ccgtacttaa ggaagg
                                                                               26
<210> 80
<211>
       26
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<220>
       PCR primer for creating a dominant negative mutant (H193L) of human histone deacetylase-3 (HDAC3) gene
<223>
<400> 80
tgtccttcct taagtacgga aattac
                                                                               26
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<211>
       22
<212> DNA
<213> Artificial
<220>
<223>
       PCR primer for creating a dominant negative mutant (H193L) of human histone deacetylase-3 (HDAC3) gene
<400> 81
gagcacaatg cacgtgggtt gg
                                                                               22
<210> 82
<211>
<212>
       29
       DNA
<213> Artificial
<220>
(223) PCR primer for amplifying RD3 sequence of human N-CoR gene
<400> 82
gggatccgtg aagtccttca gcctgctcc
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<210>
<211> 29
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<212> DNA
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 <220>
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 〈211〉
        960
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 〈220〉
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(1)..(960)
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       Corresponding to the sequence (+5281 to +6240) in the GenBank database
 <223>
        (Acession: AF196971)
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                                                                     180
 ggccactgtc cctgggtgtt cctaccccca caccctcacc ccaagacagc ctgttactgc
 ggcgccaaca gccacggtcg cctacatctg ataagactta tctgctgccc cagggcaggc
                                                                     240
                                                                     300
cggagctggc gtaagcccca gtggggcgct aagtgagtgt gcccctgcct cccgccagca
ctggcctggc ctgcaggctt agcctgggtc atcaaggtat cccacaggct ctagttcaaa
                                                                     360
tocagcagaa cotototgag cotoactott otoacotgca aaatgggtac agccacatco
                                                                     420
                                                                     480
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cacaaattaa gggctttact ctctgaaaag cccagtgaag tcatgaaacc atatctgcta
                                                                    540
                                                                    600
tittcattta tottggtttc agcctatttt gcttgtctgg acactacagt ccacgggagc
ctaggtcgag cgaggtccaa gaatccccag ggtgggcagg gagggtggaa gagggcctcc
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                                                                    720
agtgcccaag aggtgcccca caagcatggg accegcccc tcccctggac tgccccaccc
                                                                    780
gggaggaagg gagcctcaaa ggccaaggcc agccaggaca ccccctggga tcacactgag
                                                                    840
                                                                    900
cttgccacat ccccaaggcg gccgaaccct ccgcaaccac cagcccaggt cagtctcagc
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⟨210⟩
      85
      720
〈211〉
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<223>
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       (Acession: AF196971)
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cttaggcctg acggagaaga cgcgcggcca ggacacccca ccccgccct cgtctcccc
                                                                    240
aaagcctgat ctggccccac tgattccctt atctgcccac tcccagctgc ctccttgctg
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				095		
gctgaactgt	cgccgcagac	ttctgagcct	gcgccccctc	cacggggatg	ggggagggaa	300
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ggggcgccct	actcctcacc	cttggcttct	cttcctgagc	gctctgtgct	ctccagaaat	420
gaagaaatgg	ggtgagtcca	gcggccaaac	ccttgtctta	gctcttagac	atgcctcgag	480
cctgccattc	cctgtgagga	cagatttccc	tatgttgcga	ccgctgcttc	taataataat	540
aatgatgatg	ataattccca	tttacagagc	acaccattta	tggtgtgcca	gcaggccctg	600
tgctgagtgg	ttcctaccca	cgtggggggc	taggacttta	cccgttttcc	agatgaagaa	660
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<212> DNA
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<221> misc\_feature
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<223> Palindrome sequence founed on the 3' side of the GATA-E-box motif in promoter reagion of human GATA-1 gene
12

92/123